

Appl. No. : 10/041,688  
Filed : 01/07/2002

REMARKS

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

Respectfully submitted,

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Dated: \_\_\_\_\_

9/25/02

By: \_\_\_\_\_



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Deleted text is indicated by **[bracketed boldface]**. Added text is indicated by **underlined boldface**.

IN THE SPECIFICATION:

The paragraph beginning at page 2, line 25 has been amended as follows:

[Figure 1a provides schematics illustrating release of an encapsulated medicament from a cyanoacrylate adhesive matrix.] Figure 1a provides a schematic of a cross section of an adhesive matrix containing microcapsules. Figure 1b **[provides a schematic of an adhesive matrix containing both microcapsules and a defect-forming agent]**. Figure 1c provides a schematic of the solubilization of the defect-forming agent. Figure 1d] provides a schematic of the release of the microcapsules from the adhesive matrix.

The paragraph beginning at page 3, line 19 has been amended as follows:

Figure 9 provides the release curve (concentration versus time) of Sulfanilamidum from two portions of an adhesive film sample with polyethylene glycol.

The paragraph beginning at page 3, line 24 has been amended as follows:

Figures 11a and **[10b] 11b** are SEM images of the surface of a solidified adhesive containing 16.2 % PEG 600 before extraction with aqueous solution.

The paragraph beginning at page 3, line 26 has been amended as follows:

Figures 12a and **[11b] 12b** are SEM images of the surface of the adhesive of Figures 11a and **[10b] 11b** after extraction with aqueous solution.

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**The paragraph beginning at page 4, line 30 has been amended as follows:**

Any desired medicament, pharmaceutical composition, therapeutic agent, or other desired substance may be delivered to a wound that has been sealed with the disclosed adhesives. In a preferred embodiment, the medicament incorporated into the adhesive and delivered to the wound is encapsulated using known microencapsulation technologies. In other embodiments, the medicament is added directly to the adhesive. The adhesives of a preferred embodiment belong to the class of cyanoacrylate adhesives. In order to facilitate release of the medicament from the adhesive matrix, a defect or pore forming agent is formulated into the adhesive. Figure 1a provides a schematic of medicament-containing microcapsules incorporated within an adhesive matrix. The matrix may also include a defect or pore forming agent, typically a hydrophilic polymer or water soluble salt[ **(Figure 1b)**]. Upon contact with an aqueous solution (e.g., blood or tissue fluid), the defect or pore forming agent may be solubilized, leaving behind passageways into the interior of the adhesive matrix[ **(Figure 1c)**]. The microencapsulated medicament may then be released from the adhesive matrix through these defects or pores [**(Figure 1d)**] **(Figure 1b)**.

**The paragraph beginning at page 32, line 27 has been amended as follows:**

While not wishing to be limited to any particular mechanism, it is believed that when the solidified adhesive contacts an aqueous saline solution, PEG in the solid film is dissolved into the aqueous solution and leaves passage pores and defects behind. The microcapsules entrapped in the glue are thereby directly exposed to water in the channels formed by the defect generator, i.e., PEG. This process accelerates the diffusion of the antibiotic to the saline solution. Figures 11a and [10b] **11b** are SEM images of the surface of a solidified adhesive containing 16.2 % PEG 600 before extraction with aqueous solution. Figures 12a and 12b are SEM images of the surface of the same adhesive after extraction with aqueous solution. The solidified adhesive after extraction exhibits cracks and fissures not present before extraction.

**The paragraph beginning at page 37, line 25 has been amended as follows:**

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The HPLC chromatogram of an extractive solution of solidified Super Glue™ film containing DSP microcapsules is shown in Figure 19c. The peak at 10.7 min is observable[ ], indicating the release of DSP. The peak at 14.4 min is also observable, indicating that part of the DSP has decomposed during the storage of the extractive solution.

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